

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A method for evaluation of an activation state of cells in a biological sample, comprising determining an equilibrium between activities of kinase and phosphatase enzymes on specific cellular proteins participating in signal transduction into cells, said determining comprising

contacting said sample containing or suspected of containing said specific cellular proteins with two distinct arrays, said arrays comprising a plurality of capture molecules immobilized on a non-membrane solid support, said capture molecules being capable of specifically binding to both the phosphorylated and non-phosphorylated forms of the cellular proteins, wherein said specific cellular proteins are bound to the capture molecules by an epitope or site that leaves any phosphate moiety on said specific cellular protein available for detecting the level of phosphorylation,

contacting the specific cellular proteins immobilized on the first array with detection molecules being capable of specifically binding to the phosphorylated cellular proteins but not to the non-phosphorylated cellular proteins,

contacting the specific cellular proteins immobilized on the second array with detection molecules being capable of specifically binding to the phosphorylated and non-phosphorylated cellular proteins, and

quantifying the level of phosphorylation of said immobilized cellular proteins by measuring the signal ratio between the phosphorylated versus the total cellular proteins present in the sample.

2. **(Canceled)**

3. **(Canceled)**

4. **(Currently amended)** The method of Claim 1, wherein said non-membrane solid support is selected from the group consisting of: glasses, electronic devices, silicon supports, plastic supports, compact discs, and metallic supports.

5. **(Canceled)**

6. **(Canceled)**

7. **(Currently amended)** The method of Claim 1 6, wherein said capture molecules or said detection molecules or both are selected from the group consisting of: antibodies or binding parts thereof, scaffold proteins, and octamers.

8. **(Currently amended)** The method of Claim 1 5, wherein said first array and said second array are present on the same non-membrane solid support.

9. **(Currently amended)** The method of Claim 1 5, wherein said first array and said second array are present on different non-membrane solid supports.

10. **(Canceled)**

11. **(Currently amended)** The method of Claim 1 2, wherein said phosphorylation occurs on an amino acid residue selected from the group consisting of: tyrosine, serine, threonine and histidine.

12. **(Currently amended)** The method of Claim 1 2, wherein said specific cellular proteins are either involved in a biological pathway, belong to a group of proteins with identical or similar biological function, are expressed in a stage of cell cycle, expressed in a cell type, expressed in a tissue type, expressed in an organ type, or expressed in a developmental stage, proteins whose expression and/or activity is altered in a disease or disorder type or stage, or proteins whose expression, activity or a combination thereof is altered by a drug or other treatment.

13. **(Original)** The method of Claim 1, wherein said specific cellular proteins comprise at least one transcription factor.

14. **(Original)** The method of Claim 1, wherein said specific cellular proteins belong to a cascade of phosphorylation leading to an activation of at least one transcription factor.

15. **(Original)** The method of Claim 1, wherein at least 3 of said specific cellular proteins are selected from the group of proteins in Table 1.

16. **(Withdrawn)** The method of claim 15, wherein at least one of said specific cellular proteins is selected from the group of proteins provided in Table 3.

17. **(Withdrawn)** The method of Claim 15, wherein at least one of said specific cellular proteins is selected from the group consisting of: Cyclin A, Cyclin B, Cyclin D1, Cyclin D3, Cyclin E, CDK1, CDK2, CDK4, CDK6, E2F, CDC2, cdc25c, Cdc25A, Chk2, Chk1, pRb, p53, p21, p27, and Wee1.

18. **(Withdrawn)** The method of Claim 1, wherein at least 3 of said specific cellular proteins are selected from the group of proteins in Table 2.

19. **(Withdrawn)** The method of Claim 18, wherein at least one of said specific cellular proteins is selected from the group of proteins provided in Table 3.

20. **(Withdrawn)** The method of Claim 18, wherein at least one of said specific cellular proteins is selected from the group consisting of: Cyclin A, Cyclin B, Cyclin D1, Cyclin D3, Cyclin E, CDK1, CDK2, CDK4, CDK6, E2F, CDC2, cdc25c, Cdc25A, Chk2, Chk1, pRb, p53, p21, p27, and Wee1.

21. **(Withdrawn)** The method of Claim 1, wherein at least one of said specific cellular proteins is selected from the group of proteins provided in Table 3.

22. **(Currently amended)** A method for evaluation of an activation level of a cell in a test biological sample, comprising:

i) quantifying a level of phosphorylation of specific cellular proteins in said test biological sample by

contacting said sample with two distinct arrays, said arrays comprising a plurality of capture molecules immobilized on a non-membrane solid support, said capture molecules being capable of specifically binding to both the phosphorylated and non-phosphorylated forms of the cellular proteins, wherein said specific cellular proteins are bound to the capture molecules by an epitope or site that leaves any phosphate moiety on said specific cellular protein available for detecting the level of phosphorylation,

contacting the specific cellular proteins immobilized on the first array with detection molecules being capable of specifically binding to the phosphorylated cellular proteins but not to the non-phosphorylated cellular proteins,

contacting the specific cellular proteins immobilized on the second array with detection molecules being capable of specifically binding to the phosphorylated and non-phosphorylated cellular proteins, and

quantifying the level of phosphorylation of said immobilized cellular proteins by measuring the signal ratio between the phosphorylated versus the total cellular proteins present in the sample;

ii) quantifying a level of phosphorylation of said specific cellular proteins in a control biological sample, using the sub-steps outlined in step i) for the test biological sample; and

iii) comparing the level of phosphorylation of said specific cellular proteins obtained in step i) with the level of phosphorylation of said specific cellular proteins obtained in step ii), thereby identifying the activation level of said cell in said test biological sample.

23. **(Original)** The method of Claim 22, wherein said control biological sample is a normal tissue and said test biological sample is a diseased tissue.

24. **(Original)** The method of Claim 23, wherein said diseased tissue refers to a pathological condition in an organism resulting from infection or genetic defect, and is characterized by identifiable symptoms.

25. **(Original)** The method of Claim 22, wherein said control and said test biological samples are obtained from the same tissue but from different organisms, or from the same tissue at different developmental or differentiation stages of the same organism.

26. **(Original)** The method of Claim 22, wherein said control biological sample comprises untreated cells and said test biological sample comprises cells subjected to a treatment.

27. **(Currently amended)** The method of Claim 26, wherein said treatment is ~~physical, chemical, physiological or drug administration.~~

28. **(Original)** The method of Claim 22, wherein said control and said test samples comprise extracts from the same cells, and wherein said test sample comprises the extract treated in the presence of a compound to be tested.

29. **(Original)** A method for identifying a molecule affecting a level of activation of a cell, comprising:

- i) quantifying a level of phosphorylation of specific cellular proteins in a biological sample comprising said cell;
- ii) incubating said biological sample with said molecule;
- iii) quantifying a level of phosphorylation of said specific cellular proteins in said biological sample comprising said cell after step ii); and

iv) comparing the level of phosphorylation of said specific cellular proteins obtained in step i) with the level of phosphorylation of said specific cellular proteins obtained in step iii), thereby identifying the molecule affecting said level of activation of said cell.

30. **(Withdrawn)** A kit for evaluation of an activation level of a cell by quantification of a level of phosphorylation of multiple specific cellular proteins participating in signal transduction in response to a stimulus, comprising:

a support comprising a plurality of immobilized capture molecules, said capture molecules being able to specifically bind to both a phosphorylated and a non-phosphorylated forms of each of said specific cellular protein;

a first solution, comprising detection molecules able to specifically bind only to the phosphorylated forms of said specific cellular proteins;

a second solution, comprising detection molecules able to specifically bind to the non-phosphorylated forms of said specific cellular proteins; and

means for assessing the level of phosphorylation of said specific cellular proteins.

31. **(Withdrawn)** The kit of Claim 30, wherein said capture molecules are antibodies.

32. **(Withdrawn)** The kit of Claim 30, wherein said detection molecules are able to specifically bind only to the phosphorylated forms of said specific cellular protein, and said detection molecules are able to specifically bind to the non-phosphorylated forms of said specific cellular proteins are antibodies.

33. **(Withdrawn)** A support, comprising a plurality of capture molecules, said capture molecules being able to specifically bind at least 5 of the proteins from Table 1.

34. **(Withdrawn)** A support, comprising a plurality of capture molecules, said capture molecules being able to specifically bind at least 5 of the proteins from Table 2.

35. **(Withdrawn)** A support, comprising a plurality of capture molecules, said capture molecules being able to specifically bind at least 5 of the proteins from Table 3.

36. **(Withdrawn)** A support, comprising a plurality of capture molecules, said capture molecules being able to specifically bind at least 5 of the proteins selected from the group consisting of: Cyclin A, Cyclin B, Cyclin D1, Cyclin D3, Cyclin E, CDK1, CDK2, CDK4, CDK6, E2F, CDC2, cdc25c, Cdc25A, Chk2, Chk1, pRb, p53, p21, p27, and Wee1.